REMARKS

Reconsideration of this application is respectfully requested. Claims 22, 23 and 26-34 were pending in the application. Claims 22, 23, 29, 30, and 32-34 were withdrawn from consideration. Claims 26-28 and 31 are rejected. If the amendments proposed above are entered, the claims remaining for consideration will be claim 26-28. The amendments propose to cancel claims 31-34 without prejudice, and to amend claim 26. Support for the amendments can be found in lines 1-3 on page 38, and in line 23 on page 42 through line 19 on page 45. Further support can be found in lines 4-5 on page 6. Thus, claims 26 through 28 are still pending. No new matter has been added by way of this amendment. Accordingly, entry of the above amendments is believed to be in order and is requested.

The amendments proposed herein for the claims are clearly indicated in the attachment entitled "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

I. Rejections Under 35 USC § 112, first paragraph.

Claims 26-28 were rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time that the application was filed, had possession of the claimed invention. In particular, the presently pending claims recite use of an anti-DEC antibody. The specification discloses an anti human DEC antibody and an anti murine DEC antibody. Thus, the claims would encompass use of an anti DEC antibody which binds DEC from any species of animal. Applicants have amended claim 26 to focus on only anti-human or anti-murine DEC antibodies. Although Applicants believe that sufficient support has been provided to Examiner in response to the first Office Action in order to overcome this rejection, Applicants have amended claim 26 to limit the claim to human or murine antibodies to put the application in condition for allowance.

The same rejection has been made against claims 26-28 with respect to the recitation of the use of a carbohydrate that binds DEC. While applicants dispute the examiner's contention

that there is no disclosure in the specification as to the identity of any carbohydrate that actually binds DEC, applicants propose to amend the claim to delete reference to the carbohydrates that bind DEC. This amendment is suggested to facilitate early allowance and is made without prejudice to applicants' right to pursue the deleted subject matter in a continuing application.

II. Rejections Under 35 USC § 112, Second Paragraph.

Claims 26-28 and 31 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. In particular, the examiner considers claim 26 indefinite in the recitation of "dendritic and epithelial cell (DEC)" ligand. The examiner has suggested that this rejection could be addressed by the addition of description of the physical characteristics of the molecule (*e.g.* molecular weight, etc.). Accordingly, applicants have amended claim 26 to refer to a specific DEC molecule having a molecular weight of 205 kDa (*eg.* DEC-205). Support for this can be found on page 16, lines 16 through 20, wherein "DEC" is defined as an integral membrane protein found primarily on dendritic cells, B cells, brain capillaries, bone marrow stroma, epithelia of intestinal villi, and pulmonary airways, as well as cortical epithelium of the thymus and dendritic cells in the T cell areas of peripheral lymphoid organs. Moreover, applicants have indicated on page 16, lines 26-28 that because the protein has been found predominantly on **D**endritic cells and thymic **E**pithelial **C**ells, and has a molecular weight of **205** kDa, it has been termed **DEC-205**.

III. Rejections Under 35 USC § 103(a)

Claims 26-28, and 31 stand rejected under 35 U.S.C. 103(a) as obvious over Nemazee (U.S. Patent No. 5,698,679) in view of Kraal et al. As this rejection may pertain to the claims, particularly if amended as proposed, it is traversed.

Applicants request that the arguments distinguishing the references that were presented in the response to the first Office Action be incorporated herein in their entirety. Furthermore, in reference to the examiner's argument that the NLDC-145 binds DEC, Applicants note that the

opposite is in fact, confirmed to be true when an analysis was done to assess the reactivity of the Kraal NLDC-145 antibody with human DEC-205. Support for this can be found in lines 15-19 on page 3 of the specification, which states that human DEC-205 is characterized by **not reacting with** monoclonal antibody NLDC-145. Further support can be found in lines 10-13, on page 45, which states that an advantage of the present invention is that the antibodies described in the instant application can be used to target molecules to **human** dendritic cells. As noted herein ... "It is recognized that this is a significant advantage, since the prior art antibody of Kraal et al. failed to recognize human DEC.". Furthermore, Applicants have amended claim 26 to include reference to the fact that the anti-human and anti-murine DEC-205 antibodies claimed in the instant application are reactive with a **human** DEC-205 protein. Support for this can be found in lines 4-5 on page 6 of the specification.

The Kraal et al. reference as a whole. Kraal et al. describe the monoclonal antibody NLDC-145, which reacts with a 145kDa protein found on **mouse** nonlymphoid dendritic cells, including Langerhans cells, veiled cells, and interdigitating cells, but does not react with cells in the bone marrow and blood.

Kraal et al. do not disclose or suggest that the NLDC-145 antibody reacts with a specific endocytic receptor on dendritic cells and epithelial cells, as well as bone marrow cells, having a molecular weight of 205kDa, characterized as having ten lectin binding domains, and evidence of its role in the uptake and processing of oligosaccharides and oligosaccharide decorated molecules. Kraal et al. does not show that NLDC-145 could bind a receptor that mediates antigen uptake into dendritic cells and antigen presentation by these cells. Moreover, for almost 20 years after Kraal et al., Applicants' discovery of *in vivo* targeting was not carried out, due to failure to recognize and appreciate the problem. As stated in applicants' response to the first Office Action, it is critical to the present invention that DEC-205 be used to target antigens efficiently and selectively to dendritic cells and for purposes of antigen presentation on MHC class I and II products. Likewise, this criticality is applicable to human DEC-205, which is the subject of the present claims.

The analysis under § 103(a). Kraal et al did not describe the NLDC-145 antibody as being reactive with **human** DEC-205 protein. Moreover, it was not until Applicants' present invention that the identity of **human** DEC-205 and its significance as an endocytic receptor became known. Applicants' own work, as described in the instant application, clearly point out that the molecule identified by the NLDC-145 antibody was not a full length, complete DEC molecule. In fact, it was Applicants' own investigative work which identified the discrepancy in the size of the full length DEC molecule as recognized by their own antibodies, compared to the smaller 145kDa protein described by Kraal et al., for which no function was known at the time.

Furthermore, Kraal et al. do not describe the binding of NLDC-145 to **human** DEC; they merely identify the binding of a **mouse** 145kDa protein using their antibody. Nor does Kraal show that NLDC-145 could bind a receptor that mediates antigen uptake into dendritic cells and antigen presentation by these cells. Moreover, for almost 20 years after Kraal et al., Applicants' discovery of *in vivo* targeting was not carried out, due to failure to recognize and appreciate the problem. One cannot contemplate or suggest a solution without recognition of the problem.

Thus, the connection between the work done by Kraal et al. could not have been made in light of the Nemazee patent, since the identity of **human** DEC-205 was unknown at the time.

Furthermore, **since the Kraal antibody NLDC-145 does not react with human DEC-205**, as noted by the present Applicants, it would not have been obvious to one skilled in the art at the time the invention was made to combine this knowledge with the teachings of Nemazee et al.

Applicants respectfully request reconsideration of the 103(a) rejection for the following additional reasons. Applicants provide support for the different binding characteristics of the Kraal antibody vs the anti- DEC antibodies described in the present application. Applicants provide support for those differences in the specification on page 3, lines 15-19, wherein it is stated that the human DEC protein, described as having the carboxy terminal sequence provided as SEQ ID NO:1, is characterized by binding to a rabbit polyclonal antibody raised against full length murine DEC-205, but does not react with monoclonal antibody NLDC-145 (the Kraal antibody). Further support is found in lines 12-13 on page 45 which also states that the antibody

of Kraal failed to recognize human DEC. Yet further support can be found in the specification in lines 4-5 on page 6, where it is noted that the invention of the present application provides for a monoclonal and a polyclonal antibody that is reactive with a human DEC-205 protein.

Conclusion

Applicants believe that the outstanding rejections based on 35 U.S.C. §112 and 35 U.S.C. § 103(a) have been overcome by the amendments presented above. Thus, reconsideration and withdrawal of the outstanding grounds of rejection, and early allowance of the claims as amended is believed to be in order and is courteously solicited.

In the event that there are any questions concerning this amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned at the number listed below, so that prosecution of the application may be expedited.

Respectfully submitted,

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Enclosure: VERSION WITH MARKINGS TO SHOW CHANGES MADE

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26. (Twice Amended) A vaccine for inducing an immune response comprising an antigen from a pathogen conjugated to a Dendritic and Epithelial Cell-205 (DEC-205) ligand, wherein the DEC-205 ligand is [selected from the group consisting of a carbohydrate that binds DEC and] an anti-human DEC-205 antibody or an anti-murine DEC-205 antibody reactive with a human DEC-205 protein and an immune stimulator.